Epidemiology

Volume 12, Number 1

January 2001

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EDITORIALS

Frequent Radiation Exposures and Frequency-Dependent Effects: The Eyes Have It

Research into the health effects of radiofrequency radiation (RFR) has lagged the rapid growth in use of communication technologies based on this part of the electromagnetic spectrum.[1–3] Existing safety standards are intended to provide protection from thermal effects, such as burns and cataracts, which are associated with acute, high-dose exposures.[1,2] Such exposures are uncommon in the general population, in contrast to the chronic, low dose-rate exposures experienced by a large and growing segment of the public, namely, users of cellular (mobile) telephones. Whether there are any health risks associated with non-thermal, low dose-rate exposures, apart from interference with medical devices,[4] is unknown. Given the pervasiveness of cell phone use, even small health risks would be of considerable public health importance. Of all of the hypothesized adverse effects of RFR, cancer has elicited the greatest concern. Interest has centered on tumors of the brain and nervous system and hematopoietic and lymphatic tissue.[2,3,5–7] The paper by Stang and colleagues[8] in this issue is unusual in its focus on uveal (intraocular) melanoma, the most common type of eye cancer among adults.[9] The authors report elevated relative risk estimates associated with a history of employment in occupations involving use of selected RFR transmitting devices, including cellular telephones and portable, two-way radios. Of interest here is the strength of the evidence that the association is causal.

Radiofrequency radiation (300 Hz-300 GHz), including microwave radiation, encompasses a broad range of frequencies intermediate between extremely low frequency (ELF) fields at the lower end and infrared radiation at the upper end (Figure 1). Solar radiation includes RFR, but at very low power densities, and exposure to RFR is essentially a man-made phenomenon of the past century.[3,10] Sources of exposure include cellular telephones, VHF and UHF two-way radios, cordless phones, AM and FM radio, VHF and UHF television, microwave ovens, magnetic resonance imaging systems, video display terminals, anti-theft devices and security alarms, induction heaters and heat sealers, radar and satellite communications.[1,3,5,6,11] Cellular telephones operate within the 800 to 960 MHz and 1.4 to 2.2 GHz bands, and portable radios operate in several

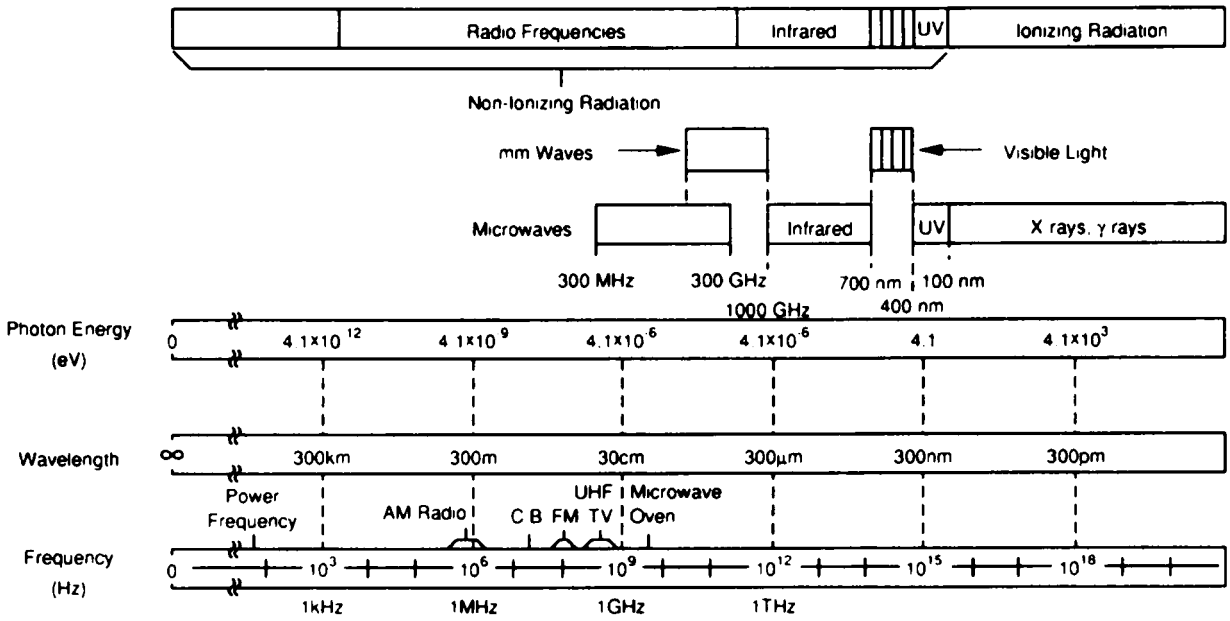

FIGURE 1. Electromagnetic spectrum. Reproduced from National Council on Radiation Protection and Measurements, Bethesda, Maryland, 1993,[1] with permission of the publisher.

bands, including 450 to 512 MHz.[1,6,12] Frequencies from 806 to 890 MHz formerly were used for UHF TV channels 70 to 83.[1]

By way of comparison, the frequency of ultraviolet radiation (UVR) is of the order of 1 to 10 million times higher, and the frequencies of X- and γ-radiations are several orders of magnitude higher still (Figure 1).[1] Because the energy of a photon of radiation is directly proportional to its frequency, the enormous differences in frequency imply similar, orders-of-magnitude variation in the energy of the radiation.[1,10,13] Gamma-rays and X-rays are sufficiently energetic to break chemical bonds and ionize molecules. UVR does not ionize molecules but is energetic enough to cause molecular excitations resulting in structural changes in DNA that can lead to mutations. RFR can induce molecular excitations resulting in tissue heating and, possibly, influence the electrical environment of cells and behavior of free radicals,[14] but it does not damage DNA directly.[10,13,15]

Notably missing from the paper by Stang *et al.* is any consideration of occupational or recreational exposure to UVR. Exposure to UVR is virtually universal, and UVR is a generally accepted cause of cutaneous melanoma.[16,17] Uveal melanoma is considerably less common and less studied than cutaneous melanoma, and there are differences in epidemiologic patterns that might reflect differences in etiology.[18] There are, however, noteworthy similarities as well, and associations between the incidence of ocular melanoma and exposure to UVR have been reported in several studies.[19–24] Sailors, welders and farmers have been reported to be at high risk, and all three groups are potentially exposed to intense or prolonged UVR.[21,25] Exposure to sun lamps and fluorescent lights also has been linked to increased risk, as has a history of nonmelanoma skin cancer,[22] a type of cancer for which the association with UVR is not in dispute. Intermittent, intense exposure, such as that associated with sunburns, appears to be more important than chronic or cumulative exposure, at least for some types of melanoma, and occupational groups at highest risk are not necessarily those who spend the most time outdoors.[16,22,26–28] Overall, the reverse seems to be true, with a higher relative risk associated with indoor work than outdoor work, and with higher rather than lower social class.[29,30]

The likely etiologic importance of UVR has been questioned on the grounds that little UVR penetrates the cornea and lens to reach the choroid, where most uveal melanomas arise.[31,32] The lens, however, transmits some long wavelength UVR in adults and a much higher proportion of 300–400 nm UVR in children.[10,33,34] It also is possible that UVR carcinogenicity is mediated through a systemic effect, such as on the immune system.[35–37] Although the role of UVR (or other forms of solar radiation) in the etiology of ocular melanoma is an unsettled issue, UVR is a stronger candidate, on *a priori* grounds, than RFR or ELF and merits consideration as part of a study concerning the risk of uveal melanoma associated with "... occupational exposures to different sources of electromagnetic radiation ..." [sic] [see Abstract].

As with UVR, the depth of penetration of RFR in tissue varies inversely with frequency.[1,2,5,10] Very high frequency RFR is absorbed almost entirely at the surface of the skin, where it produces heating. Very low frequency RFR penetrates tissue but does not cause heating; instead, it induces electric currents and fields. RFR of the intermediate frequencies used by cellular phones

and portable radios is attenuated rapidly with passage through tissue.[6] The level of RFR reaching the highly vascularized choroid would be insufficient to raise temperature above background levels. The mechanism by which non-thermal doses of RFR might cause cancer is unknown. Neither ionizing radiation nor UVR serve as a good model, as both of these established carcinogens are genotoxic, and even brief exposures can pose a risk. A variety of possible non-genotoxic, carcinogenic effects of RFR have been hypothesized, many of which involve potentiation of effects due to other agents.[14]

Stang *et al.* speculate that RF radiation might act as a cancer promoter, by inhibiting melatonin production by cells in the retina and ciliary body, which, in turn, might remove a block to proliferation of potentially cancerous cells. This parallels Stevens'[38] hypothesis concerning breast cancer and ELF fields. Nevertheless, exposure to ELF fields was not associated with risk of uveal melanoma in the present study, nor was exposure to video display terminals or radar. The authors do not explain why they would expect RFR associated with use of cellular phones or radio sets to be more effective in suppressing melatonin secretion than ELF fields, visible light, or low or high frequency RFR. The relative importance of melatonin production in the eye (choroid) versus in the pineal gland also is unclear. de Seze *et al.*[39] did not observe evidence of altered melatonin levels in circulating blood associated with use of cellular phones.

Speculation about possible mechanisms seems a bit premature, given the limitations of the study and the lack of corroborative evidence in the literature. The authors note that their study was part of a much larger effort to study risk factors for eight different cancer sites and was not designed to address RFR exposures in particular; hence, the lack of a detailed RFR exposure assessment. Intensity of exposure could not be addressed, and there was no power for assessing either duration of exposure or latency. The overall odds ratio of 3.0 associated with use of radio sets or mobile phones was based on a total of 16 exposed cases. Information was not available concerning domestic use of cellular phones or tumor laterality relative to side of phone use. There are potentially important occupational exposures beyond those considered.[1,5,11,40] Swerdlow[41] observed that "poor measurement both diminishes the capability of studies to determine whether there is an association of RF with risk of disease and, if a raised risk is found, to judge whether the association is causal."

If Stang *et al.*'s hypothesis is correct, and use of a cellular phone increases the risk of uveal melanoma appreciably, then one would expect the incidence to increase over time. Most informative would be data for countries or regions with longer histories of widespread, heavy cellular phone use. Unlike cutaneous melanoma, the incidence of ocular melanoma remained relatively stable during the latter half of the 20th century.[18,42] If there has been a recent increase due to use of cellular phones, it is less likely to be mixed in with a longer term secular trend due to some other factor.

At present, there is no strong reason to believe that RFR causes cancer, but there is only a very limited epidemiologic literature on which to base evaluations. The extent of public exposure and concern requires that the question be investigated further. Stang and colleagues raise the possibility that we should add a new type of cancer to those already under leading consideration as possible hazards of RFR, and it may well be that future studies will support their hypothesis. At this point, however, given the small size of their study, the relatively crude exposure assessment, the absence of attention to UVR exposure or other possible confounding variables, and limited support in the literature, a cautious interpretation of their results is indicated.

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References

1. NCRP (National Council on Radiation Protection and Measurements). A practical guide to the determination of human exposure to radiofrequency fields. NCRP Report No. 119; National Council on Radiation Protection and Measurements, Bethesda, Maryland, 1993.
2. Repacholi MH. Low-level exposure to radiofrequency electromagnetic fields: health effects and research needs, Bioelectromagnetics 1998;19:1–19.
3. Elwood J. A critical review of epidemiologic studies of radiofrequency exposure and human cancers. Environ Health Perspect 1999;107(suppl 1):155–168.
4. Hayes DL, Wang PJ, Reynolds DW, et al. Interference with cardiac pacemakers by cellular telephones. N Engl J Med 1997;336:1473–1479.
5. WHO (World Health Organization). Electromagnetic fields (300 Hz to 300 GHz). Geneva: World Health Organization, 1993;290 pages.
6. Rothman KJ, Chou CK, Morgan R, Balzano Q, Guy AW, Funch DP, et al. Assessment of cellular telephone and other radio frequency exposure for epidemiologic research. Epidemiology 1996;7:291–298.
7. Morgan RW, Kelsh MA, Zhao K, Exudies KA, Herringer S, Negrete W. Radiofrequency exposure and mortality from cancer of the brain and lymphatic/hematopoietic systems. Epidemiology 2000;11:118–127.
8. Stang A, Anastassiou G, Ahrens W, Bromen K, Bornfeld N, Jöckel K-H. The possible role of radiofrequency radiation in the development of uveal melanoma. Epidemiology 2001;12:7–12.
9. Parkin DM, Whelan SL, Ferlay J, Raymond L, Young J, eds. Cancer Incidence in Five Continents. vol. 7. IARC Scientific Pub. No. 143. Lyon: International Agency for Research on Cancer, 1997.
10. Lerman S. Radiant Energy and the Eye. New York: Macmillan, 1980.
11. Mantiply ED, Pohl KR, Poppell SW, Murphy JA. Summary of measured radiofrequency electric and magnetic fields (10 kHz to 30 Ghz) in the general and work environment. Bioelectomagnetics 1997;18:563–577.
12. Millington RJ. Mobile and personal communications in the 90s. In: Kuster N, Balzano Q, Lin JC, eds. Mobile Communications Safety. New York: Chapman and Hall, 1997;3–9.
13. Valberg PA. Radio frequency radiation (RFR): the nature of exposure and carcinogenic potential. Cancer Causes Control 1997;8:323–332.
14. Adey WR. Bioeffects of mobile communications fields: possible mechanisms for cumulative dose. In: Kuster N, Balzano Q, Lin JC, eds. Mobile Communications Safety. New York: Chapman and Hall, 1997;95-131.
15. Brusick D, Albertini R, McRee D, Peterson D, Williams G, Hanawalt P, Preston J. Genotoxicity of radiofrequency radiation. DNA/Genetox Expert Panel. Environ Mol Mutagen 1998;32:1–16.
16. Elwood JM, Jopson J. Melanoma and sun exposure: an overview of published studies. Int J Cancer 1997;73:198–203.
17. Langley RGB, Sober AJ. A clinical review of the evidence for the role of ultraviolet radiation in the etiology of cutaneous melanoma. Cancer Invest 1997;15:561–567.
18. Egan KM, Seddon JM, Glynn RJ, Gragoudas ES, Albert DM. Epidemiologic aspects of uveal melanoma. Surv Ophthalmol 1988;32:239–251.
19. Tucker MA, Shields JA, Hartge P, Augsburger J, Hoover RN, Fraumeni JF Jr. Sunlight exposure as risk factors for intraocular malignant melanoma. N Engl J Med 1985;313:789–792.

20. Holly EA, Aston DA, Char DH, Kristiansen JJ, Ahn DK. Uveal melanoma in relation to ultraviolet light exposure and host factors. Cancer Res 1990; 50:5773–5777.
21. Holly EA, Aston DA, Ahn DK, Smith AH. Intraocular melanoma linked to occupations and chemical exposures. Epidemiology 1996;7:55–61.
22. Seddon JM, Gragoudas ES, Glynn RJ, Egan KM, Albert DM, Blitzer PH. Host factors, UV radiation, and risk of uveal melanoma. A case-control study. Arch Opthalmol 1990;108:1274–1280.
23. Horn EP, Hartge P, Shields JA, Tucker MA. Sunlight and risk of uveal melanoma. J Natl Cancer Inst 1994;86:1476–1479.
24. Li W, Judge H, Gragoudas ES, Seddon JM, Egan JM. Patterns of tumor initiation in choroidal melanoma. Cancer Res 2000;60:3757–3760.
25. Saftlas AF, Blair A, Cantor KP, Hanrahan L, Anderson HA. Cancer and other causes of death among Wisconsin farmers. Am J Ind Med 1987;11:119–129.
26. Fears TR, Scotto J, Schneiderman MA. Mathematical models of age and ultraviolet effects on the incidence of skin cancer among whites in the United States. Am J Epidemiol 1977;105:420–427.
27. Beral V, Robinson N. The relationship of malignant melanoma, basal and squamous skin cancers to indoor and outdoor work. Br J Cancer 1981;44: 886–891.
28. Armstrong BK. Epidemiology of malignant melanoma: intermittent or total accumulated exposure to the sun. J Dermatol Surg Oncol 1988;14:835–849.
29. Lee JAH, Strickland D. Malignant melanoma: social status and outdoor work. Br J Cancer 1980;41:757–763.
30. Elwood JM, Hislop TG. Solar radiation in the etiology of cutaneous malignant melanoma in Caucasians. Natl Cancer Inst Monogr 1982;62:167–171.
31. Lerman S. Sunlight and intraocular melanoma. N Engl J Med 1986;314: 712–713.
32. Schwartz LH, Ferrand R, Boelle PY, Maylin C, D'Hermies F, Virmont J. Lack of correlation between the location of choroidal melanoma and ultraviolet-radiation dose distribution. Radiat Res 1997;147:451–456.
33. Hoover HL. Solar ultraviolet irradiation of human cornea, lens, and retina equations of ocular irradiation. Appl Opt 1986;25:359–368.
34. Gallagher RP. Ocular melanoma in farmers. Am J Ind Med 1988;13:523–525.
35. Hersey P, Haran G, Hasic E, Edwards A. Alteration of T cell subsets and induction of suppressor T cell activity in normal subjects after exposure to sunlight. J Immunol 1983;31:171–174.
36. Tucker MA, Hartge P, Shields JA. Epidemiology of intraocular melanoma. Recent Results Cancer Res 1986;102:159–165.
37. Kripke ML. Ultraviolet radiation and immunology: something new under the sun – presidential address. Cancer Res 1994;54:6102–6105.
38. Stevens RG. Electric power use and breast cancer: a hypothesis. Am J Epidemiol 1987;125:556–561.
39. de Seze R, Ayoub J, Peray P, Miro L, Touitou Y. Evaluation in humans of the effects of radiocellular telephones on the circadian patterns of melatonin secretion, a chronobiological rhythm marker. J Pineal Res 1999;27:237–242.
40. Loomis D, Browning SR, Schenck AP, Gregory E, Savitz DA. Cancer mortality among electric utility workers exposed to polychlorinated biphenyls. Occup Environ Med 1997;54:720–728.
41. Swerdlow AJ. Measurement of radiofrequency radiation exposure in epidemiological studies. Radiat Prot Dosim 1999;83:149–153.
42. Østerlind A. Trends in incidence of ocular malignant melanoma in Denmark 1943–1982. Int J Cancer 1987;40:161–164.

Is Chemical Pollution Responsible for Childhood Tumors?

In this issue of *Epidemiology*, two papers provide evidence that chemical pollutants could be responsible for some fraction of the occurrence of childhood leukemia[1] and neuroblastoma.[2] Childhood tumors are different from adult onset cancers in several ways, one of which is particularly challenging to epidemiologists: whereas for several adult-onset tumors, epidemiology and prevention have made substantially more contribution than treatment, the opposite is true for childhood tumors. For these neoplasms epidemiology and prevention have contributed little, in striking contrast to the remarkable therapeutic improvements during the last few decades for many forms of childhood malignancies, notably for childhood leukemia.[3]

Childhood Leukemia

The vast majority of childhood leukemia is acute lymphoblastic leukemia, for which there is some evidence that the incidence may be increasing slightly.[4] Little is known about its etiology except that genetic factors play a role[5] and that ionizing radiation weights more heavily in the etiology of acute lymphoblastic leukemia than in that of most other malignancies.[6,7] These causes, however, account for only a very small fraction of cases of childhood leukemia. The hypothesis that exposure to extremely low frequency electric and/or magnetic fields is responsible for a large fraction of acute lymphoblastic leukemia has only weak empirical support.[8–11] Thus, the etiology of the large majority of childhood leukemia remains unexplained. Two general hypotheses have competed for the vacuum: one focuses on viral infections, the other on chemical environmental exposures.

The central role that viruses play in leukemogenesis in several animal species and the documentation of the human T-cell leukemia/lymphoma virus in a very rare form of leukemia have lead plausibility to the hypothesis of viral leukemogenesis in children. On the other hand, there has been no laboratory support for the hypothesis, and several investigators have postulated that childhood leukemia may be only a rare outcome of a common infection in a background of low herd immunity.[12–15] In contrast, there is no theoretical undermining for a role of chemical environmental pollution in the causation of acute lymphoblastic leukemia, and this relation has not been investigated through analytical, as opposed to ecological designs.[16] The paper by Infante-Rivard *et al.* in this issue[1] presents results for what may well be the most sophisticated epidemiologic investigation to date of acute lymphoblastic leukemia in relation to drinking water contamination.

The study by Infante-Rivard *et al.*[1] is a large population-based case-control investigation that was undertaken with an elaborate protocol to evaluate the relation between childhood leukemia and drinking water contaminants, specifically total and selected trihalometh-

anes, certain metals, and nitrates. The authors developed an exposure matrix on the basis of municipal and provincial historical data and a tap water survey. None of these sources was complete with respect to any of the studied exposures, and imputations and occasionally arbitrary choices were necessary. Nevertheless, it is hard to think of a better design or a more satisfactory context for such an investigation. The authors evaluated average exposure level as well as cumulative exposure and they have focused on both the pregnancy and the postnatal period. They concluded that "the indications for an association between childhood leukemia and disinfection by-products as well as some metals are not strong, nor are they absent, in particular for postnatal exposure."

Despite the expertise and the amount of work the authors invested in this study, I do not agree completely with their conclusion. In my opinion, the study provides very little evidence for any association between the studied exposures and childhood leukemia. The authors report that there are no important differences with respect to average values for any of the studied exposures in either the prenatal or in the postnatal period. They consider notable, however, the apparent excess risk for acute lymphoblastic leukemia among children postnatally exposed to cumulative levels of total trihalomethanes, in particular, chloroform above the 95th percentile, even though the increases are trivial; they relate to a small proportion of children and they could even be due to differences *in duration* of exposure, generated by unavoidably suboptimal age-matching of cases and controls. The authors also consider as noteworthy the excess risk for acute lymphoblastic leukemia in relation to cumulative zinc levels above the 95th percentile, even though the evidence for carcinogenicity of zinc is generally minimal. Regardless of the interpretation, it is clear that the evaluated contaminants of drinking water can explain no more than a trivial fraction of the total cases of acute lymphoblastic leukemia, and possibly none at all.

Neuroblastoma

Neuroblastoma is a rare childhood tumor and yet it is the most common tumor in the 1st year of life. It derives from embryonal cells in the neural crest, and it arises in the adrenal medulla or anywhere else in the sympathetic chain. The disease appears to be less common in developing countries and among preterm babies. Neuroblastoma is accompanied by fever and weight loss; the physical examination reveals an abdominal mass. Diagnosis relies on ultrasound, computerized tomography, excretion of catecholamines in the urine and, eventually, biopsy. The prognosis of the disease is good when the tumor is detected before the first year but it is poor when the tumor is detected later in life. The aberrant expression of the MYCN oncogene is considered a marker of poor prognosis.

Few studies have evaluated the etiology of neuroblastoma. Exposure to pesticides was considered in some of them[17–21] and the collective evidence for an association with neuroblastoma appears to be supportive but far from conclusive. The study by Daniels and colleagues in this issue[2] is only the second in the literature that has relied on specific information about pesticide exposure[21] rather than on indirect evidence based on paternal job title, family residence or pesticide purchase records. The study was as strong as any, but relies on random digit dialing. The information about children's exposure to pesticides was elicited from the best possible source, the parents. The results appear to support the hypothesis that pesticide exposure increases the risk of neuroblastoma, but there are some important concerns. It is disquieting that more parental pairs disagreed about exposure to pesticides than agreed that there was indeed such an exposure; this was the case even with respect to extermination, which should be a memorable event. Moreover, information bias cannot be easily discounted in this instance, since many view pesticides with suspicion. Third, pesticides are a large and heterogeneous group, making it difficult to draw generalizable inferences.

Both studies do not provide compelling evidence for a causal link between the studied exposures and outcomes, but they do not provide much comfort either. They are important because they convey two essential messages: (1) the population rates of childhood tumors attributable to these exposures are unlikely to be high and may even be zero and (2) in this particular field, it is difficult to envisage studies more informative than these, unless susceptibility to the exposures under consideration is differentially increased or even limited to particular polymorphisms that need to be evaluated simultaneously.

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References

1. Infante-Rivard C, Olson E, Jacques L, Ayotte P. Drinking water contaminants and childhood leukemia. Epidemiology 2000;12:13–19.
2. Daniels JL, Olshan AF, Teschke K, Hertz-Picciotto I, Savitz DA, Blatt J, Bondy ML, Neglia JP, Pollock BH, Cohn SL, Look AT, Seeger RC, Castleberry RP. Residential pesticide exposure and neuroblastoma. Epidemiology 2000;12:20–27.
3. La Vecchia C, Levi F, Lucchini F, Lagiou P, Trichopoulos D, Negri E. Trends in childhood cancer mortality as indicators of the quality of medical care in the developed world. Cancer 1998;83:2223–2227
4. Wang PP, Haines CS. Childhood and adolescent leukaemia in a North American population. Int J Epidemiol 1995;24:1100–1109.
5. Crist WM, Pui C-H. The leukemias. In: Nelson Textbook of Pediatrics. 15th Edition. Eds: Behrman RE, Kliegman RM, Arvin AM. Saunders Publications. 1996:1452–1455.
6. U.S. National Academy of Sciences Committee on Biological Effects of Ionizing Radiation. Washington, DC: BEIR-V (U.S. N A.S.) 1990.
7. Petridou E, Trichopoulos D, Dessypris N, Flytzani V, Haidas S, Kalmanti M, Koliouskas D, Kosmidis H, Piperopoulou F, Tzortzatou F. Infant leukaemia after in utero exposure to radiation from Chernobyl. Nature 1996;382:352–353.
8. Linet MS, Hatch EE, Kleinerman RA, Robison LL, Kaune WT, Friedman DR, Severson RK, Haines CM, Hartsock CT, Niwa S, Wacholder S, Tarone RE. Residential exposure to magnetic fields and acute lymphoblastic leukemia in children. N Engl J Med 1997;337:1–7.

9. UK Childhood Cancer Study Investigators. Exposure to power-frequency magnetic fields and the risk of childhood cancer. Lancet 1999;354:1925–1931.
10. Repacholi MH, Albhom A. Link between electromagnetic fields and childhood cancer unresolved. Lancet 1999;354:1918–1919.
11. National Research Council. Possible health effects of exposure to residential electric and magnetic fields. National Research Council, Washington: DC: National Academy Press, 1996.
12. Kinlen LJ. Evidence for an infective cause of childhood leukaemia: comparison of a Scottish new town with nuclear reprocessing sites in Britain. Lancet 1988;II:1323–1327.
13. MacMahon B. Is acute lymphoblastic leukemia in children virus-related? Am J Epidemiol 1992;136:916–924.
14. Petridou E, Kassimos D, Kalmanti M, Kosmidou H, Haidas S, Flytzani V, Tong D, Trichopoulos D. Age of exposure to infections and childhood leukemia risk. BMJ 1993;307:774.
15. Greaves MF. Aetiology of acute leukemia. Lancet 1997;349:344–349.
16. Foster AM, Prentice AG, Copplestone JA, Cartwright RA, Ricketts C. The distribution of leukaemia in association with domestic water quality in south west England. Eur J Cancer Prevention 1997;6:11–19.
17. Kristensen P, Andersen A, Irgens LM, Bye AS, Sundhem L. Cancer in offspring of parents engaged in agricultural activities in Norway: Incidence and risk factors in the farm environment. Int J Cancer 1996;65:39–50.
18. Bunin GR, Ward E, Kramer S, Rhee CA, Meadows AT. Neuroblastoma and parental occupation. Am J Epidemiol 1990;131:776–780.
19. Spitz MR, Johnson CC. Neuroblastoma and parental occupation. Am J Epidemiol 1985;21:924–929.
20. Wilkins JR, Hundley VD. Paternal occupational exposure to electromagnetic fields and neuroblastoma in offspring. Am J Epidemiol 1990;131:995–1107.
21. Michaelis J, Haaf HG, Zollner J, Kaatsch P, Krummenauer F, Berthold F. Case control study of neuroblastoma in West-Germany after the Chernobyl accident. Klin Padiatr 1996;208:172–178.